Devices and CBER: 2006 Update

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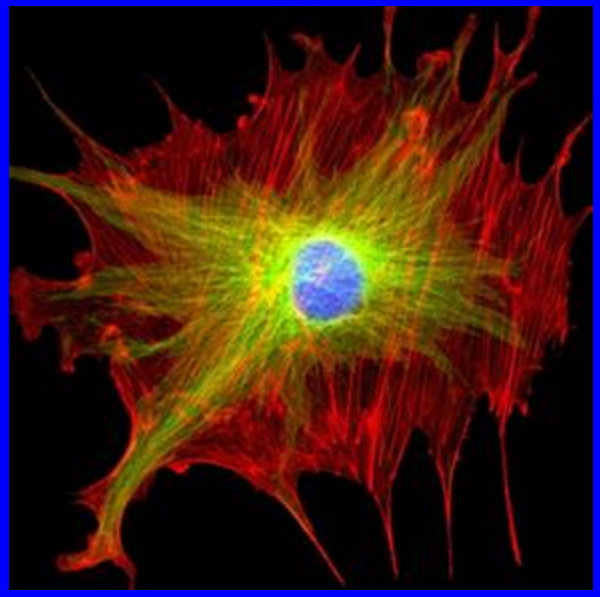
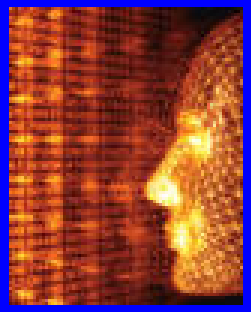
AdvaMed, March 4, 2006

Purpose

- **Share and discuss:**
  - **CBER vision, mission, selected public health accomplishments**
  - **Device performance and related updates**
  - **Recent CBER and FDA Initiatives of interest to AdvaMed members**

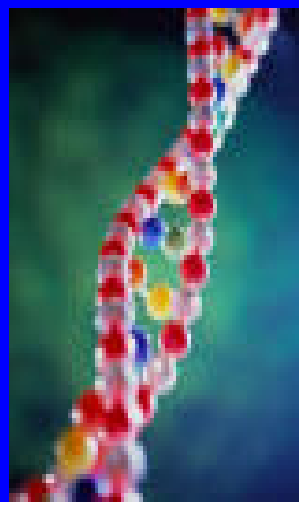




Vision for CBER

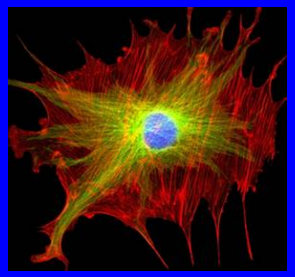
INNOVATIVE TECHNOLOGY ADVANCING PUBLIC HEALTH

- **Protect and improve public and individual health in the US and, where feasible, globally**
- **Facilitate the development, approval and access to safe and effective products and promising new technologies**
- **Strengthen CBER as a preeminent regulatory organization for biologics**



Mission: Complex Products Critical for Public Health, National Preparedness & 21st Century Medicine

Blood



Almost all areas involve medical devices in product availability or delivery

CBER Products Touch Everyone's Lives and Are Essential to Current and Future Health Care

- More than 235 million vaccinations each year to prevent serious infectious diseases, e.g., Hib
- ~ 30 million blood & component transfusions
- One million tissues (e.g., bone, skin, ligaments) transplanted last year to repair injury, restore function and improve quality of life
- 800 active human studies of cell, gene, tissue/tissue engineering, vaccine and blood products for treatment or prevention of serious diseases, e.g., HIV, cancer, diabetes, heart disease

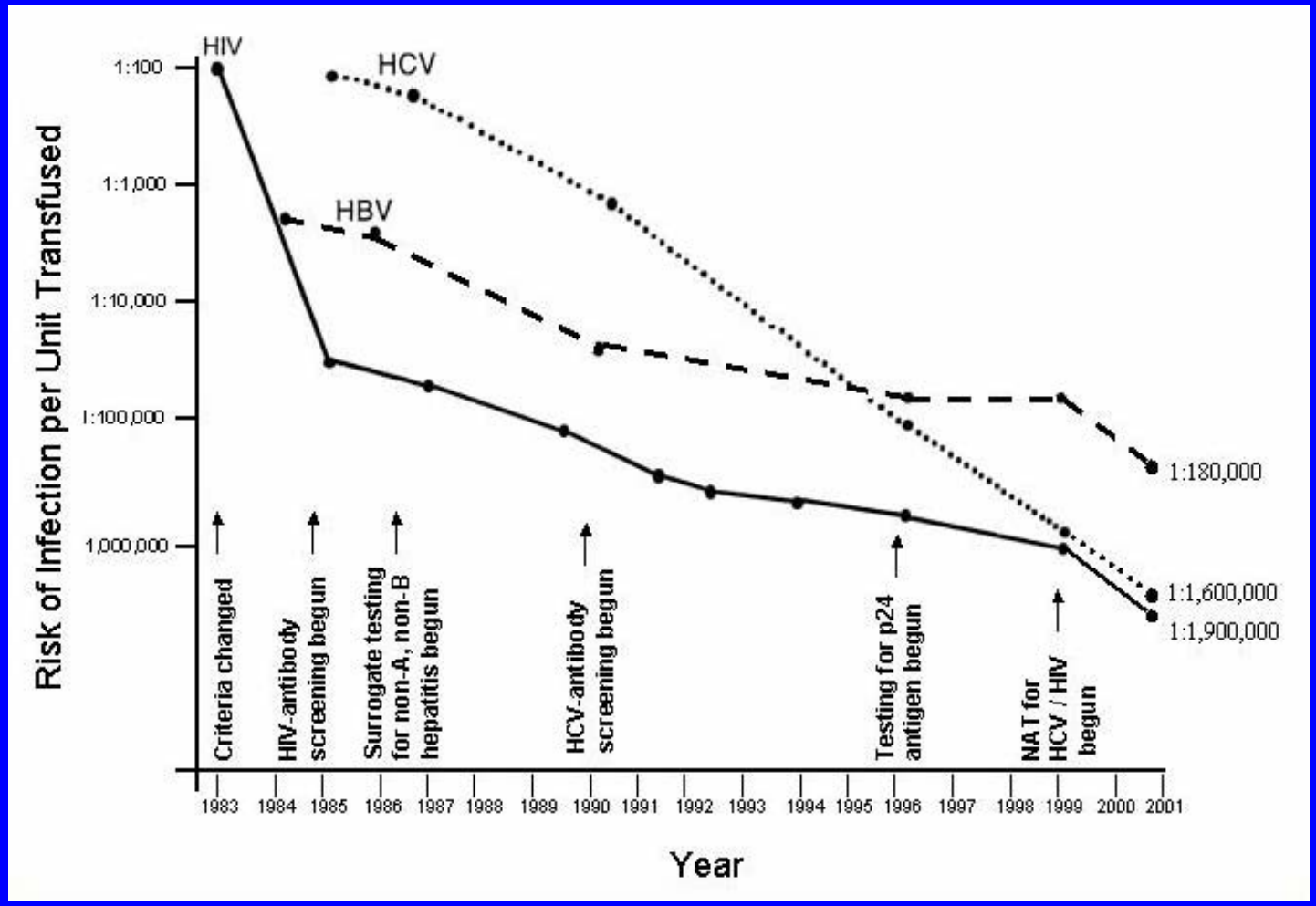
Not Business as Usual

- Since 9/11, CBER has adapted to extraordinary circumstances through extraordinary efforts
  - These include proactive measures w/ sister agencies and industry such as:
    - **Meetings to encourage and speed developing needed new products**
    - **Early and intensive ongoing interactions w/ sponsors**
    - **Collaboration and rapid turnaround in product review**
    - **Proactive trips to inspect facilities**
    - **Participation in multiple product development teams**
    - ***Critical Path Research: Focused, proactive research targeted to more efficient, rapid product development and availability***
  - Such approaches were used in West Nile response and in the 2004 flu season and inform all our current activities (for example pandemic preparedness).

Selected Recent Public Health Accomplishments

- **Assuring Product Safety & New Product Pathways**
  - **Guidances: TSE, NAT, UDHQ, gene and cell therapies, influenza vaccines (annual and pandemic)**
- **Important new products to patients – examples**
  - ***HIV Rapid Test – oral fluid***
  - ***New blood screening tests for HIV, hepatitis B, West Nile***
  - ***7d platelet storage containers to work with detection systems***
  - ***Pooled platelet container***
  - ***Blood compatibility testing***
  - **First combination whooping cough vaccine for adolescents**
  - **Menactra to prevent meningitis**
  - **Fluarix accelerated approval**
  - **New rotavirus vaccine (global and US health)**
- **CT and Emergency Preparedness**
  - **Vaccinia, botulinum immune globulins**
  - **First BioShield Emergency Use Authorization**

CBER Approved Tests You Developed Have Made Blood Transfusions Safer



New Threats: West Nile Virus and Blood and Tissue Safety

- **Problem: A new threat to blood safety, human to human WNV transmission by blood transfusion and transplantation was first identified in 2002 by CDC and FDA working together**
- **Actions: FDA articulated the need to develop and implement testing and convened an unprecedented collaborative effort with CDC, NIH and the blood and diagnostic industries**
- **FDA articulated criteria for approval pathway of WNV NAT assays and helped develop and provide needed reference materials**
- **2003: Implementation of nationwide screening blood supply using investigational NAT assays (less than 8 months from first detection)**
- **FDA and device industry have coordinated with CDC, NIH and blood banking establishments to monitor data on WNV and evaluate testing.**
- **Outcomes: NAT screening prevented distribution of > 1,600 infected units, reducing spread of WNV and death to blood recipients, blood screening serves as disease surveillance tool as well**
- **Licensed NAT screening now available for blood, tissues and organs**
- **Comment: *We need next generation tests; more automation, multiplexing, flexibility***

CBER Device Application Receipts

FY 2002 – FY 2006*

		MDUFMA			
	FY02	FY03	FY04	FY05	FY06*
PMAs (Traditional)	0	0	0	3	3
PMAs (Modular)	1	3	1	2	0
PMSs (180 Day)	5	3	3	2	1
510(k)s (All Types)	40	65	78	63	15
BLAs (Original)	2	0	9	15	0
BLSs (Efficacy)	0	3	0	0	0
BLSs (Manuf, PAS)	35	75	96	45	13

*Data through January 31, 2006

CBER: Reinvention of Device Review

Receipt to Final Action

FY 2002-FY 2006*

		MDUFMA			
	FY02	FY03	FY04	FY05	FY06*
CBER Review Time (days)	122.5	59.2	67.5	69.8	49.1
Average Number of Cycles	1.8	1.4	1.4	1.4	1.0

Includes SEs/NSEs; WDs are not included

*Data through January 31, 2006

MDUFMA Performance
510(k) Applications

Goal: Decision within 90 total FDA days

	1st QTR FY 04	2nd QTR FY 04	3rd QTR FY 04	4th QTR FY 04	Annual Totals FY 04
Total Received	18	21	26	13	78
Total Filed	18	21	26	13	78
Meeting Goal	17	20	21	12	70 (97%)
Not Meeting Goal	--	1	--	1	2 (3%)
Awaiting MDUFMA Decision	--	--	--	--	--

FY 2004 Cohort

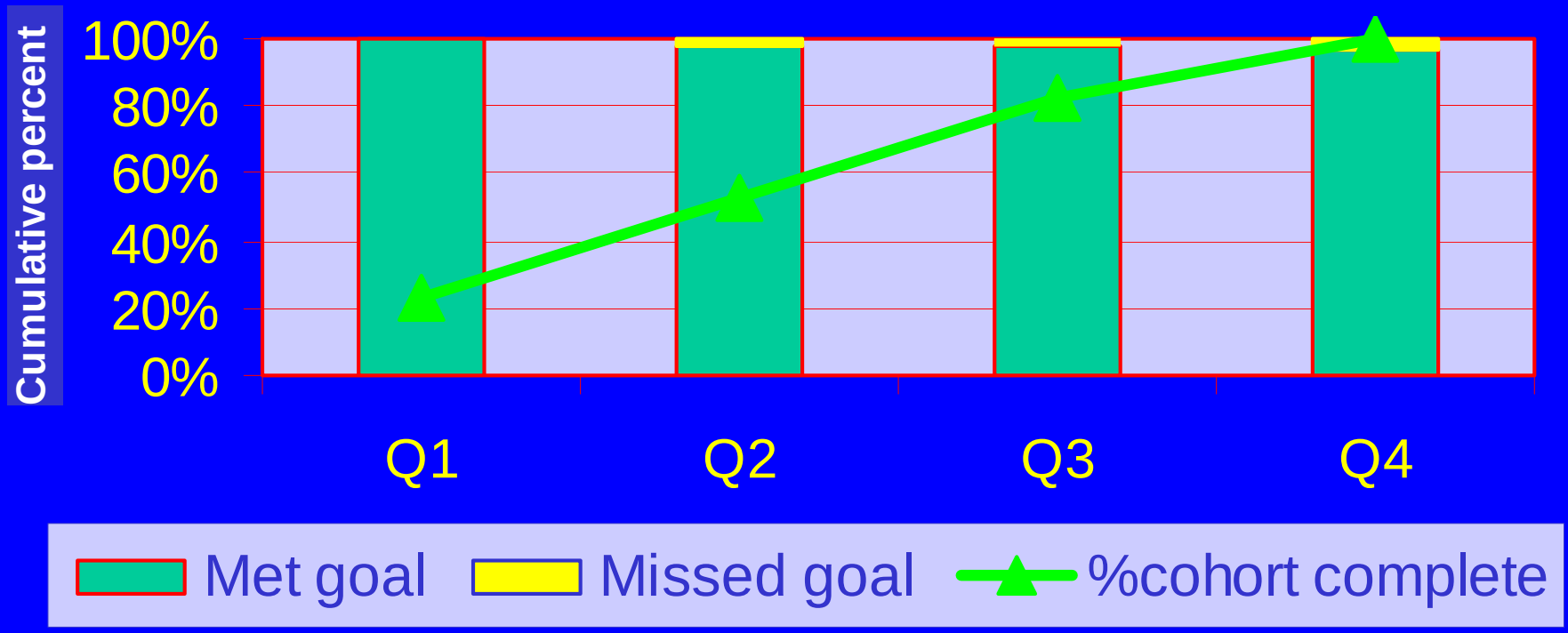
(as of 1/31/06)

** - Goals and Decisions do not include three 510(k) application withdrawals by the applicants and three exemptions.

(D-329)RIMS:2/21/06

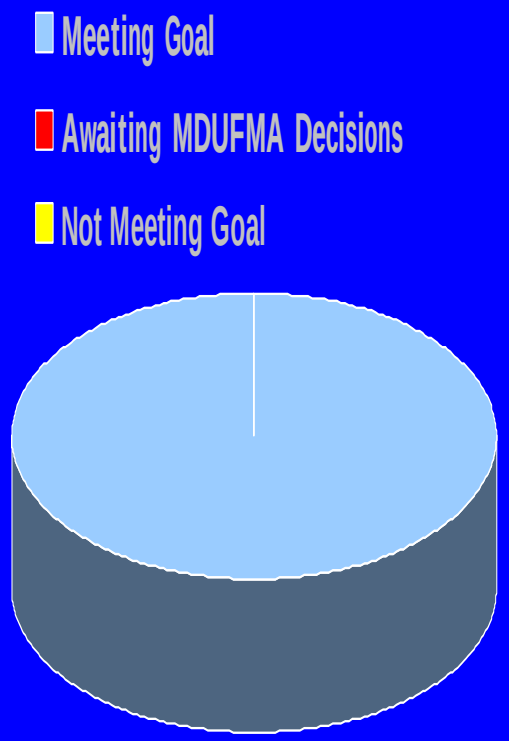
510k FY 2004 Receipt Cohort

Final Decisions



MDUFMA Performance
Original PMAs and PMA Panel Track Supplements
Goal: Decision within 320 total FDA days

	1st QTR FY 04	2nd QTR FY 04	3rd QTR FY 04	4th QTR FY 04	Annual Totals FY 04
Total Received	0	0	1	0	1
Total Filed	--	--	1	--	1
Meeting Goal	--	--	1	--	1 (100%)
Not Meeting Goal	--	--	--	--	--
Awaiting MDUFMA Decision	--	--	--	--	--

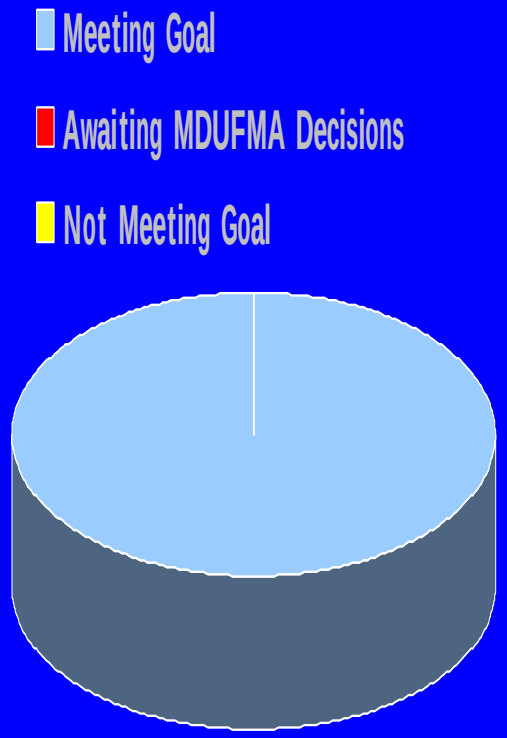


FY 2004 Cohort

(as of 1/31/06)

MDUFMA Performance
180-Day PMA Supplements
Goal: Decision within 180 total FDA days

	1st QTR FY 04	2nd QTR FY 04	3rd QTR FY 04	4th QTR FY 04	Annual Totals FY 04
Total Received	2	0	1	0	3
Total Filed	2	--	1	--	3
Meeting Goal	2	--	1	--	3 (100%)
Not Meeting Goal	--	--	--	--	--
Awaiting MDUFMA Decision	--	--	--	--	--



FY 2004 Cohort

(as of 1/31/06)

MDUFMA Performance
Biologics License Applications
Goal: First action within 10 months total FDA time

	1st QTR FY 04	2nd QTR FY 04	3rd QTR FY 04	4th QTR FY 04	Annual Totals FY 04
Total Received	1	5	2	1	9
Total Filed	1	5	2	1	9
Meeting Goal	1	5	2	1	9 (100%)
Not Meeting Goal	--	--	--	--	--
Awaiting MDUFMA Decision	--	--	--	--	--

FY 2004 Cohort

(as of 1/31/06)

MDUFMA Performance
BLA Prior Approval Manufacturing Supplements
Goal: First action within 4 months total FDA time

	1st QTR FY 04	2nd QTR FY 04	3rd QTR FY 04	4th QTR FY 04	Annual Totals FY 04
Total Received	5	29	32	30	96
Total Filed	5	29	32	30	96
Meeting Goal	5	29	32	30	96 (100%)
Not Meeting Goal	--	--	--	--	--
Awaiting MDUFMA Decision	--	--	--	--	--

FY 2004 Cohort

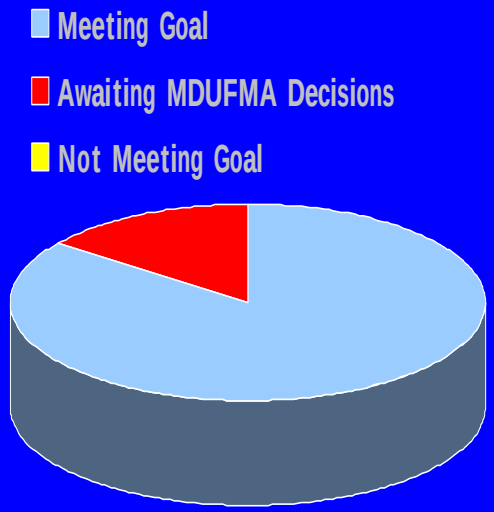
(as of 1/31/06)

(D-333) RIMS:2/21/06

MDUFMA Performance
510(k) Applications

Goal: Decision within 90 total FDA days

	1st QTR FY 05	2nd QTR FY 05	3rd QTR FY 05	4th QTR FY 05	Annual Totals FY 05
Total Received	13	15	14	21	63
Total Filed	13	15	14	21	63
Meeting Goal	12	14	10	16	52 (85%)
Not Meeting Goal	--	--	--	--	--
Awaiting MDUFMA Decision	1	1	3	4	9 (15%)



FY 2005 Cohort

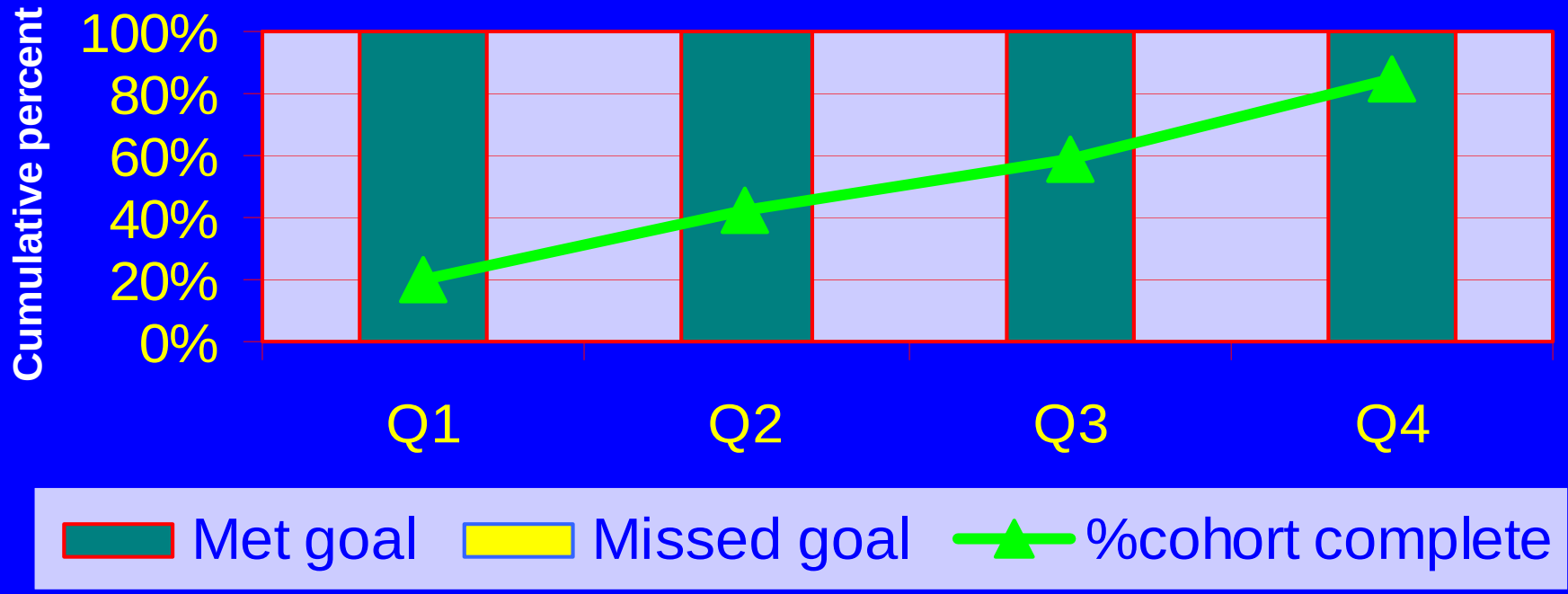
(as of 1/31/06)

** - Goals and Decisions do not include two withdrawals by the applicants.

(D-390)RIMS:2/21/06

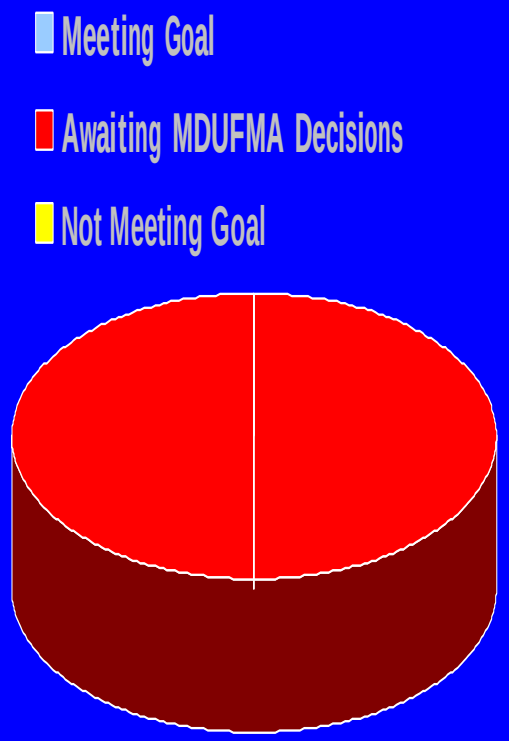
510k FY 2005 Receipt Cohort

Final Decisions



MDUFMA Performance
Original PMAs and PMA Panel Track Supplements
Goal: Decision within 320 total FDA days

	1st QTR FY 05	2nd QTR FY 05	3rd QTR FY 05	4th QTR FY 05	Annual Totals FY 05
Total Received	1	2	1	1	5
Total Filed	1	2	1	1	5
Meeting Goal	--	--	--	--	--
Not Meeting Goal	--	--	--	--	--
Awaiting MDUFMA Decision	1	2	1	1	5 (100%)



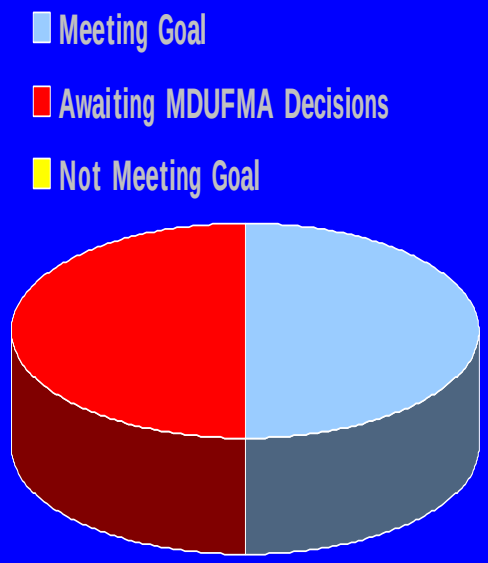
FY 2005 Cohort

(as of 1/31/06)

MDUFMA Performance
180-Day PMA Supplements

Goal: Decision within 180 total FDA days

	1st QTR FY 05	2nd QTR FY 05	3rd QTR FY 05	4th QTR FY 05	Annual Totals FY 05
Total Received	0	1	0	1	2
Total Filed	--	1	--	1	2
Meeting Goal	--	1	--	--	1 (50%)
Not Meeting Goal	--	--	--	--	--
Awaiting MDUFMA Decision	--	--	--	1	1 (50%)



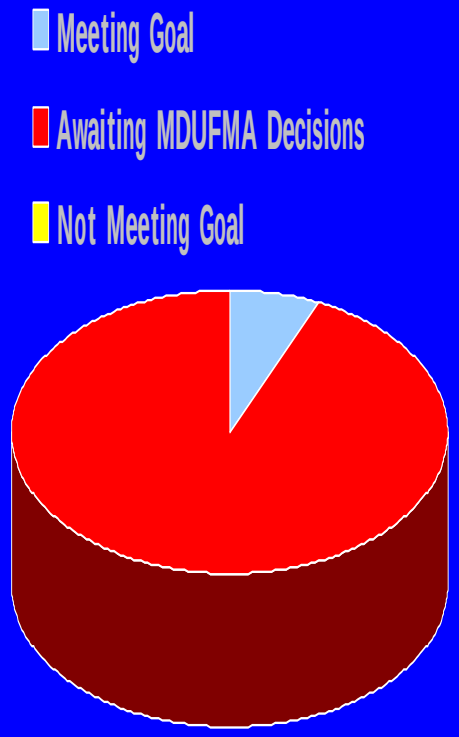
FY 2005 Cohort

(as of 1/31/06)

MDUFMA Performance
Biologics License Applications

Goal: First action within 10 months total FDA time

	1st QTR FY 05	2nd QTR FY 05	3rd QTR FY 05	4th QTR FY 05	Annual Totals FY 05
Total Received	0	1	14	0	15
Total Filed	--	1	14	--	15
Meeting Goal	--	1	--	--	1 (7%)
Not Meeting Goal	--	--	--	--	--
Awaiting MDUFMA Decision	--	--	14	--	14 (93%)

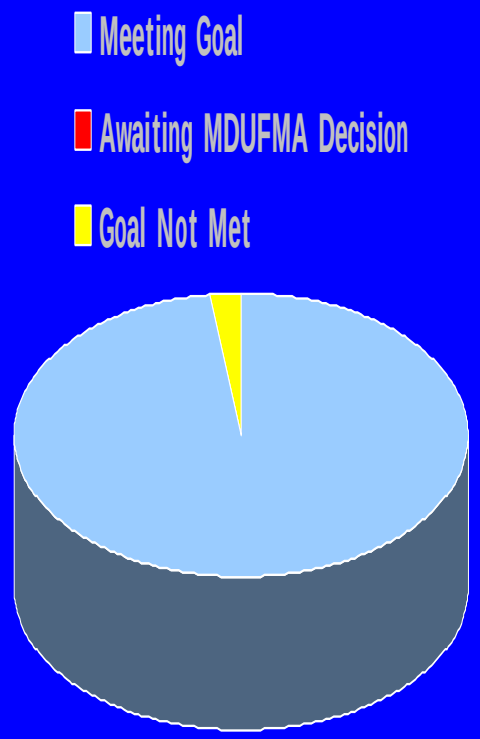


FY 2005 Cohort

(as of 1/31/06)

MDUFMA Performance
BLA Prior Approval Manufacturing Supplements
Goal: First action within 4 months total FDA time

	1st QTR FY 05	2nd QTR FY 05	3rd QTR FY 05	4th QTR FY 05	Annual Totals FY 05
Total Received	6	6	28	5	45
Total Filed	6	6	28	5	45
Meeting Goal	6	6	28	4	44 (98%)
Not Meeting Goal	--	--	--	1	1 (2%)
Awaiting MDUFMA Decision	--	--	--	--	--



FY 2005 Cohort

(as of 1/31/06)

CBER DEVICE RESOURCES

Pre and Post MDUFMA

	FY 2002 (pre-MDUFMA)	FY 2003	FY 2004	FY 2005
MDUFMA FTE Effort	45.0	59.5	66.6	80
TOTAL FTE Effort	56.0	69.2	75.1	98.8

* Includes surveillance & enforcement, laboratory.

Managed Device Review Process

- Continued High Level Oversight & Support
- Medical device reviewer training 2x/year, plus specialized training
  - e.g., 2006 CBER-CDRH cartilage seminars
- Device Review Subcommittee of Review Management Coordinating Committee
  - Establishes CBER device processes and policies
  - Issues Center level SOPPs http://www.fda.gov/cber/regsopp/regsopp.htm
  - SOPPs updated & consistent w/ CDRH bluebook
- Extensive CBER/CDRH collaboration
  - Bidirectional review consultation, TRG, tissue engineering, policy, Device Subcommittee WG

Sustainability in Device Review

Continue to support innovation in review

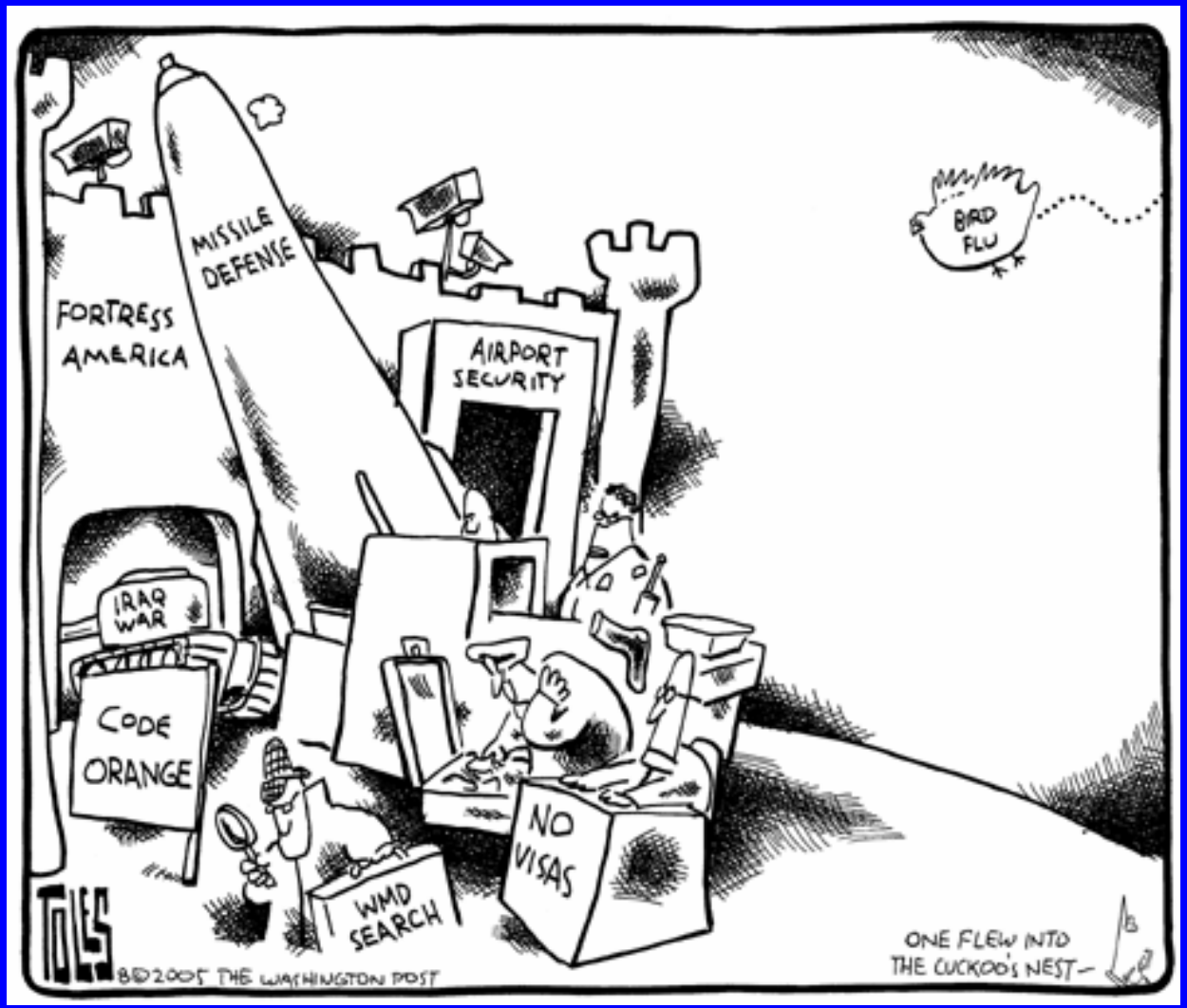
- **Mid-cycle reviews**
- **Enhanced and earlier/informal communication**
- **Templates**
- **Increased QA/QC**
- **Organizational strengthening and training in management and review**

– Continuing to support MDUFMA and apply MDUFMA resources to efforts is critical

Active Device Outreach

- MATES, NBIB
- Orthopedics; AAOS Device Forum
- OCRA, AMDA
- Liaison Meetings, e.g, AdvaMed
- Blood Sector and IVD Roundtable
- Stakeholders meetings

Challenges and Initiatives



2006 CBER Initiatives/Issues of Special Interest to AdvaMed

- Pandemic Preparedness
- Integrated Safety Teams and Safety Surveillance
- Tissues and Tissue Engineering Team
- Product Evaluation Labs and Quality Systems
- Expert Consultants
- Critical Path

Meeting the Pandemic Flu Vaccine Challenge: Overview and Actions

- ✓ Increasing manufacturing diversity & capacity
- ✓ Developing needed pathways and regulatory processes to speed vaccine availability
- ✓ Assuring safety and public confidence
- ✓ Facilitating vaccine manufacturing/availability
  - ✓ enabling current and evolving technologies
  - ✓ assisting landmark effort to produce/evaluate H5N1 vaccine (manufacturing, reagents etc.)
  - – antigen sparing: adjuvants and delivery
- ✓ Considering pathways to prevent a pandemic
- ✓ Global assistance, cooperation, harmonization

Integrated Product Safety Teams

- Bring together all involved in product safety across organizations and organizational components as well as linking relevant data across systems – using standard operational procedures
  - CBER: clinical and product reviewers, epidemiologists/adverse event reports/reviews, risk science, compliance & inspectional activities, manufacturing and inspection reports, communications
  - Partners: CDC, NIH, other Centers, ORA, industry
- Encompass entire product life cycle, use health care databases actively
- Proactive: set research, policy, outreach agendas
- Emergency response leadership and coordination
- Tissue pilot success: blood, vaccine teams in 06

Tissues

- **Patient Safety- Tissues**
  - **Tissue Safety Framework**
    - **Finalization of Donor Suitability & GTP Rules: DONE!**
    - **CBER/CDC collaboration and EIS Fellows**
  - ***Tissue Safety Team* formed including all offices**
    - **SOPs to facilitate reporting/receipt/investigation of AEs**
    - **Active surveillance one ultimate goal**
    - **Development of shared databases**
    - **Liaison with ORA, CDC, and HRSA**
    - **Training, outreach, inspection and compliance**

Meeting *New* Needs - Tissues

- **Goals**
  - Assuring safe tissues for transplantation and as starting materials for complex products (combination, tissue engineering)
  - Timely transition from discovery to innovative and consistent products
- **Gaps**
  - Basic scientific knowledge still emerging; novel approaches needed to product development, characterization and regulatory assessment
  - Tissue safety: new risk based approach, implementation and scientific needs include better rapid testing, product sterilization, preservation
- **Progress**
  - CBER Tissue Safety Team - discussed
  - Interdisciplinary MATES strategic plan for tissue engineering
  - CBER/CDRH review and science team for tissue engineered products

CBER/CDRH Tissue Engineering Team 06 Priorities

- Timely and excellent cross-center collaborative reviews
- Efficient resolution of issues in master files that may result in clinical holds
- Joint guidance on knee cartilage repair products
- Increased role in standards development for tissue engineering products (ASTM, ISO)
- Strong FDA voice in MATES (Multi-agency Tissue Engineering Science)
- Outreach in tissue engineering/regenerative medicine
- Develop strategies for characterization of cell/scaffold products to help promote efficient product development

- **Enhance Performance of Product Evaluation Laboratories**
  - Leveraging resources and infrastructure to pilot move of influenza related testing and technologies to model centralized quality system and ISO certification
  - Creating methods evaluation and validation group
    - Can work bi-directionally with stakeholders, including industry
  - Will benefit all product testing through better facilities, quality systems, increased ability to promote use of new technologies, and enhanced leadership and management
- **Facilitate and Increase Use of Expert Consultants**
  - CBER has increased use of expert consultants generally, both inside and outside FDA
  - In 2006 will create an expertise database and support the use of outside consultants by reviewers

Critical Path: Building a Bridge from Discovery Research to Better Health

- FDA/CBER focus is to identify solutions to product development challenges: tools and pathways to help cross the bridge from discovery to products - **different** from basic biomedical discovery
- As a "final common pathway" scientific expertise is essential in translating basic biotech into real medical therapies for people, assuring they are safe, and helping keep them available – realizing the promise of 21st Century medicine and making a difference in people's lives – *shared goals with AdvaMed*

CBER Science for Critical Path

- ***SAFER, BETTER PRODUCTS FASTER TO IMPROVE PUBLIC HEALTH, NATIONAL PREPAREDNESS, AND PATIENTS' LIVES***
  - **Potency/effectiveness/standards**
    - » **Biomarkers, surrogates, animal models, standards**
  - **Safety**
  - **Consistency/manufacturing/quality**
  - **Needed policy and guidance**
- ***Especially high impact and importance where incentives weak – public health, counterterrorism, emerging infectious diseases, uncertain or niche markets, high risk/novel technologies: includes most CBER devices***
- ***Preserve a science led FDA: global gold standard/leader***

Critical Path Science Investment & Partnership Opportunities: Examples

- **Develop/make available well characterized cell banks (and methods to assay for safety/adventitious agents) for biologics production – & update guidance**
- ***Characterization of cell therapies & links to standardized clinical/lab outcomes***
- ***New assays, standards, biomarkers, surrogates for biologics safety, efficacy and quality***
- ***Methods & validation of pathogen inactivation for blood, plasma, tissues and other products (e.g. TSE)***
- ***Multipathogen, unique pathogen and rapid detection methodologies, including nanotech***
- ***Improving longevity/storage of blood and tissues***
- ***Enhanced clinical trial design/analysis***

Thank you

- **We are proud of our staff and our role in public health, biodefense and the development & availability of new products for the 21st century**
- **New technologies, including devices, need expert, innovative, interactive review, regulation and science, new models, standards, assays – CBER devices should be important in "Critical Path"**
- ***Together we can build bridges to turn discoveries into products to better lives –safer, better, faster***
- **We see a positive future with exciting products**

focus
innovate
succeed

Contact me: jgoodman@cber.fda.gov
or at 301-827-0372

CBER: INNOVATIVE TECHNOLOGY ADVANCING PUBLIC HEALTH